

Amendments to the Claims

Claim 1 (Currently amended): An isolated oligonucleotide ~~sequence~~ which encodes a synthetic suppressor tRNA comprising:

- A) a human tRNA structural gene sequence comprising no more than twenty 3' flanking residues and no 5' flanking residues, said sequence encoding an anticodon region for pairing with mRNA;
- B) an anticodon sequence contained within said anticodon region which has been modified to recognize a codon different from that which is originally recognized;

wherein said oligonucleotide has a total length of less than 150 nucleotides.

Claim 2 (Original): A synthetic suppressor tRNA molecule encoded by the oligonucleotide of claim 1.

Claim 3 (Currently amended): The oligonucleotide of claim 1 wherein said anticodon region ~~encodes~~ recognizes ~~[[an-]]~~ a nonsense mutation selected from the group consisting of: amber (TAGUAG), ochre (UAA) and opal (UGA).

Claim 4 (Currently amended): The oligonucleotide of claim 1 ~~further comprising a second oligonucleotide sequence as described in claim 1 wherein said two sequences are in tandem~~ wherein said oligonucleotide encodes said synthetic suppressor tRNA in tandem.

Claim 5 (Original): The oligonucleotide of claim 1 wherein said tRNA structural gene sequence encodes a serine tRNA.

Claim 6 (Original): The oligonucleotide sequence of claim 1 wherein said tRNA structural gene sequence encodes an arginine tRNA.

Claim 7 (Currently Amended) An oligonucleotide which encodes a synthetic suppressor tRNA comprising:

- A) a human tRNA structural gene sequence comprising no more than twenty 3' flanking residues and no 5' flanking residues, said sequence encoding an anticodon region for pairing with mRNA;
- B) an anticodon sequence contained within said anticodon region which has been modified to recognize a codon different from that which is originally recognized;

wherein said oligonucleotide has a sequence selected from the group consisting of SEQ ID NOS:1-10 ~~and their complements~~ and wherein said oligonucleotide has a total length of less than 150 nucleotides.

Claim 8 (Previously presented): A method of restoring translation to a nucleotide sequence which includes a nonsense mutation in a cell comprising:

introducing to said cell a nucleic acid sequence which encodes a synthetic suppressor tRNA oligonucleotide, said oligonucleotide comprising:

- A) a human tRNA structural gene sequence comprising no more than twenty 3' flanking residues and no 5' flanking residues, said sequence encoding an anticodon region for pairing with mRNA;
- B) an anticodon sequence contained within said anticodon region which has been modified to recognize a codon different from that which is originally recognized, wherein said

anticodon is one which will pair with said nonsense mutation and said tRNA structural gene sequence encodes an amino acid which is deleted by said nonsense mutation; wherein said oligonucleotide has a total length of less than 150 nucleotides.

Claim 9 (Original): The method of claim 8 wherein said nucleotide sequence with said nonsense mutation is one which has been introduced to said cell.

Claim 10 (Previously Presented): The method of claim 8 wherein said tRNA structural gene sequence encodes a serine tRNA.

Claim 11 (Previously Presented): The method of the oligonucleotide claim 8 wherein said tRNA structural gene sequence encodes an arginine tRNA.

Claim 12 (Currently amended): The method of claim 8 wherein said oligonucleotide has a sequence selected from the group consisting of SEQ ID NOS:1-10 and their complements.

Claim 13 (Currently amended): A method of restoring translation to a nucleotide sequence which includes a nonsense mutation in a cell comprising:
introducing to said cell a synthetic suppressor tRNA oligonucleotide, said oligonucleotide being one which is encoded by the ~~sequence~~ oligonucleotide of claim 1.

Claim 14 (Currently amended): A nucleotide vector comprising the ~~nucleotide sequence~~ oligonucleotide of claim 1.

Claim 15 (Original): The nucleotide vector of claim 14 wherein said vector is a viral vector.

Claim 16 (Original): The vector of claim 14 wherein said vector is a viral vector selected from the group consisting of:
a retroviral, adenoviral, adeno-associated, Herpes simplex virus and Herpes simplex viral vector.

Claim 17 (Original): The vector of claim 14 wherein said vector is a Herpes virus vector.

Claim 18 (Original): The vector of claim 14 wherein said vector is a Herpes virus mini amplicon vector comprising:
an Epstein-Barr virus ori P and EBNA-1 sequence to maintain the plasmid episomally, a hygromycin resistance gene, an HSV-1 lytic replication origin (ori S), and a HSV-1 terminal packaging signal.

Claim 19 (Original): The vector of claim 14 wherein said vector is the *pHhargsup* tRNA^{Opal} vector.

Claim 20 (Currently amended): A transformed host cell comprising the ~~nucleotide sequence~~ oligonucleotide of claim 1.

Claim 21 (Original): A transformed host cell comprising the synthetic suppressor tRNA molecule of claim 2.

Claim 22 (Currently amended): A method for ~~introducing site specific mutation to~~
suppressing the effect of nonsense mutations in a translated protein nucleotide sequence
encoding a protein comprising:

introducing to said cell a nucleic acid sequence which encodes a synthetic suppressor tRNA
oligonucleotide, said oligonucleotide comprising:

- A) a human tRNA structural gene sequence comprising no more than twenty 3' flanking
residues and no 5' flanking residues, said sequence encoding an anticodon region for
pairing with mRNA;
- B) an anticodon sequence contained within said anticodon region which has been modified
to recognize a codon different from that which is originally recognized, wherein said
anticodon is one which will pair with said nonsense mutation and said tRNA structural
gene sequence encodes an amino acid which is deleted by said nonsense mutation;

wherein said oligonucleotide has a total length of less than 150 nucleotides.

Claim 23 (Currently amended): The method of claim 22 wherein said anticodon region
~~encodes-recognizes~~ [[aa-]] a nonsense mutation selected from the group consisting of:
amber (TAGUAG), ochre (UAA) and opal (UGA).

Claim 24 (Previously Presented): The method of claim 22 wherein said tRNA structural gene
sequence encodes a serine tRNA.

Claim 25 (Previously Presented): The method of claim 22 wherein said tRNA structural gene sequence encodes an arginine tRNA.

Claim 26 (Previously Presented): The method of claim 22 wherein said oligonucleotide has a sequence selected from the group consisting of SEQ ID NOS:1-10 and their complements.

Claim 27 (Currently amended): A method for ~~introducing site specific mutation~~
~~to suppressing the effect of nonsense mutations in a translated protein nucleotide sequence~~
~~encoding a protein~~ comprising:
introducing to said ~~a cell~~ bearing such a nonsense mutation a synthetic suppressor tRNA encoded
by the ~~sequence-oligonucleotide~~ of claim 1.

Claim 28-31 (Canceled).

Claim 32 (Currently amended): A method of ~~correcting genetic defects~~ changing
translational products in animals a cell comprising:
introducing to said animal a suppressor tRNA sequence, said tRNA sequence comprising:
A) a human tRNA structural gene sequence comprising no more than twenty 3' flanking
residues and no 5' flanking residues, said sequence encoding an anticodon region for
pairing with mRNA;
B) an anticodon sequence contained within said anticodon region which has been modified
to recognize a codon different from that which is originally recognized;
wherein said oligonucleotide has a total length of less than 150 nucleotides.

Claim 33 (Currently amended): The method of claim 32 wherein said anticodon region ~~encodes~~ recognizes an nonsense mutation selected from the group consisting of:
amber (TAGUAG), ochre (UAA) and opal (UGA).

Claim 34 (Previously Presented): The method of claim 32 wherein said tRNA structural gene sequence encodes a serine tRNA.

Claim 35 (Previously Presented): The method of claim 32 wherein said tRNA structural gene sequence encodes an arginine tRNA.

Claim 36 (Currently amended): The method of claim 32 wherein said oligonucleotide has a sequence selected from the group consisting of SEQ ID NOS:1-10 ~~and their complements~~.

Claim 37 (Original): The method of claim 32 wherein said disease is Xeroderma Pigmentosum.

Claim 38 (Currently amended): A method of monitoring transduction of cells comprising:
introducing to said cells ~~and an~~ oligonucleotide vector comprising a reporter gene said reporter gene having been inactivated by introduction of a nonsense mutation;
introducing to said cells ~~a suppressor tRNA sequence~~ an oligonucleotide which encodes a synthetic suppressor tRNA according to claim 1; and
assaying for reactivation of the reporter gene.

Claim 39 (Original): The method of claim 38 wherein said reporter gene is selected form the group consisting of: chloramphenicol acetyl transferase and green fluorescent protein.